REMARKS

Claims 1-3 and 6-13 are pending in the present application and under examination. Claims 4 and 5 are canceled. Claim 13 is amended herewith. Support for the amendment may be found throughout the specification, including by way of example on page 5, lines 34-35. Therefore no new matter is introduced with this amendment. In the Office Action mailed on August 27, 2009, all of the claims were rejected.

I. Rejection Under 35 USC § 101

Claim 13 is rejected under 35 U.S.C. § 101 as allegedly being unpatentable because the claimed invention is directed to a non-statutory subject matter. Claim 13 has been amended rendering the rejection moot.

Applicants therefore respectfully request the withdrawal of the rejection of claim 13.

II. Rejections Under 35 USC § 103

Claims 9-11 and 13 are rejected under 35 U.S.C. § 103(a) as being unpatentable (1) over Wang et al. (WO2002077183, October 3 2002) in view of Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pgs 53-137, 1989) and (2) over Tettelin et al. (Science, 287: 1809-1815, 2000; of record on 1449) in view of Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pgs 53-137, 1989) and Campbell (Monoclonal Antibody Technology, Chapter 1 pages 1-32, Elsevier Science Publishing Company, Inc., 1986, section 1.3.4).

Claim 12 is rejected under 35 U.S.C. § 103(a) as being unpatentable (1) over Wang et al. (WO2002077183, October 3 2002) and Harlow and Lane (Antibodies a Laboratory Manual) as applied to claims 9-11 and 13 above and further in view of Telford et al. (WO 02/34771 May 2, 2002) and (2) over Tettelin et al. (Science, 287: 1809-1815, 2000), Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pgs 53-137, 1989) and Campbell

(Monoclonal Antibody Technology, Chapter 1 pages 1-32, Elsevier Science Publishing Company, Inc., 1986, section 1.3.4) as applied to claims 9-11 and 13 above and further in view of Telford et al. (WO 02/34771, May 2 2002).

Applicants respectfully traverse the rejections and their supporting remarks.

A. Rejections Based on Wang et al.

Wang et al. as cited by the Examiner, fail to render the pending claims obvious. The Example 12 as identified by the Examiner is a prophetic example of generating antibodies against large genus of polypeptides "including one of the polypeptides of SEQ ID NOs.: 42398-78581." The Examiner asserts that '(i)t would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the protein or 15-mer derived there from of Wang et al. with an adjuvant in order to make antibodies according to Wang et al. because Harlow et al. and Wang et al. teach that adjuvants can boost the immune response to protein antigens.'

However, in order to be obvious, a compound that is suggested to be made must have a "specific or significant" utility. The utility guidelines for patentable inventions provide useful guidance as to what constitutes a "substantial utility," which defines a "real world" use for the invention [MPEP § 2107.01 (I)(B)]. The MPEP § 2107.01 (I)(B) further states:

> the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> (A)Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
>
> (B)A method of treating an unspecified disease or condition;
>
> (C)A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
>
> (D)A method of making a material that itself has no specific, substantial, and credible utility; and
>
> (E)A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

The only reasons provided by Wang et al. for the production of antibodies are:

> Antibody preparations prepared according to either protocol [generation of monoclonal or polyclonal antibodies] are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies can also be used in therapeutic compositions for killing bacterial cells expressing the protein. (pg. 1529, WO 02/077183)

These reasons do not qualify as real world utilities under MPEP § 2107.01 (I)(B). Indeed, Wang et al.'s stated reasons for producing antibodies fall precisely within the defined situations listed above which according to the MPEP do not qualify as 'substantial utilities.' In particular, Wang's statement that the antibodies can be used to determine the concentration of antigens in a biological sample at least falls under MPEP § 2107.01 (I)(B)(C) ('A method of assaying for or identifying a material that itself has no specific and/or substantial utility') since Wang et al. fail to teach a reason for quantifying any of the over 36,000 cited polypeptides much less selecting the one that the Examiner has alleged has 99.2% identity to the presently claimed SEQ ID NO: 207 (and applicants respectfully traverse and request that the Examiner provide the sequence alignment and SEQ ID NO of the polypeptide corresponding to "essential gene #23372" or to "essential gene #13372" as the Examiner uses both numbers). Furthermore, simple logic dictates that the one potential utility of detecting a bacterial infection would not likely be met by any of the over 36,000 cited polypeptides as these genes were identified as being "essential". If these polypeptides are truly essential, then they will also be essential to the non-pathogenic variants. By way of example *Neisseria flavescens* SK114 is a commensal relative of *N. meningitidis*. The following alignment shows that this commensal organism has a close homolog of NMB1799 (available from the Uniprot data base as C5TL4 - ~97% identity).

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NMB1799: MSEYLFTSESVSEGHPDKVADQVSDAILDAILAQDPKARVAAETLVNTGLCVLAG  1-55
       : MSEYLFTSESVSEGHPDKVADQVSDAILDAILAQD KARVAAETLVNTGLCVLAG
C5TL49 : MSEYLFTSESVSEGHPDKVADQVSDAILDAILAQDLKARVAAETLVNTGLCVLAG  1-55

NMB1799: EITTTAQVDYIKVARETIKRIGYNSSELGFDANGCAVGVYYDQQSPDIAQGVNEG  56-110
       : EITTTAQVDYIKVARETIKRIGYNSSELGFDANGCAVGVYYDQQSPDIAQGVNEG
C5TL49 : EITTTAQVDYIKVARETIKRIGYNSSELGFDANGCAVGVYYDQQSPDIAQGVNEG  56-110
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NMB1799: EGIDLNQGAGDQGLMFGYACDETPTLMPFAIYYSHRLMQRQSELRKDGRLPWLRP  111-165
       : EGIDLNQGAGDQGLMFGYACDETPTLMPFAIYYSHRLMQRQSELRKDGRLPWLRP
C5TL49 : EGIDLNQGAGDQGLMFGYACDETPTLMPFAIYYSHRLMQRQSELRKDGRLPWLRP  111-165

NMB1799: DAKAQLTVVYDSETGKVKRIDTVVLSTQHDPSIAYEELKNAVIEHIIKPVLPSEL  166-220
       : DAKAQLTVVYDS+TGKVKRIDTVVLSTQHDPSI YEELKNAVIEHIIKPVLPSE+
C5TL49 : DAKAQLTVVYDSKTGKVKRIDTVVLSTQHDPSIGYEELKNAVIEHIIKPVLPSEM  166-220

NMB1799: LTDETKYLINPTGRFVIGGPQGDCGLTGRKIIVDTYGGAAPHGGGAFSGKDPSKV  221-275
       : LTDETKYLINPTGRFVIGGPQGDCGLTGRKIIVDTYGGAAPHGGGAFSGKDPSKV
C5TL49 : LTDETKYLINPTGRFVIGGPQGDCGLTGRKIIVDTYGGAAPHGGGAFSGKDPSKV  221-275

NMB1799: DRSAAYACRYVAKNIVAAGLATQCQIQVSYAIGVAEPTSISIDTFGTGKISEEKL  276-330
       : DRSAAYACRYVAKNIVAAGLATQCQIQVSYAIGVAEPTSISIDTFGTGKISEEKL
C5TL49 : DRSAAYACRYVAKNIVAAGLATQCQIQVSYAIGVAEPTSISIDTFGTGKISEEKL  276-330

NMB1799: IALVREHFDLRPKGIVQMLDLLRPIYSKSAAYGHFGREEPEFTWERTDKAAALRA  331-385
       : IALVREHFDLRPKGIVQMLDLLRPIYSKSAAYGHFGREEPEFTWERTDKAAAL+A
C5TL49 : IALVREHFDLRPKGIVQMLDLLRPIYSKSAAYGHFGREEPEFTWERTDKAAALKA  331-385

NMB1799: AAGL  386-389
       : AAG+
C5TL49 : AAGV  386-389
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Thus, one of skill in the art could not use antibodies to NMB1799 to differentiate between a non-pathogenic bacteria which is known to colonize the nasopharnyx of humans versus *N. meningitidis*. Thus one of skill in the art would not be motivated to select "essential gene #23372" from among all the other polypeptides to generate antibodies as such antibodies would not be able to determine whether a patient was infected with *N. meningitidis* or was simply colonized by a commensal bacteria.

Further, Wang's statement that the antibodies can be used as therapeutic compositions for killing bacteria also fails to have a real utility in the case of "essential gene #23372". One of skill in the art would recognize that therapeutic antibodies can only work when the protein recognized is on the surface of the bacteria. NMB1799 was not annotated as a membrane protein and in fact was annotated as a metabolic protein "S-adenosylmethionine synthetase", which one of skill in the art would not expect to be immunoaccessible (i.e., surface exposed) (See page 40, lines32-24 of the specification). Therefore, any antibodies generated as described by Wang et al. would be expected to lack a substantial utility, and without a substantial utility, one of skill in the art would not be motivated to actually select "essential gene #23372" from among over 36,000 polypeptides to make

antibodies. Rather, one of skill in the art would expressly ignore "essential gene #23372" and would search for a polypeptide that was known to be surface exposed.

This is clearly discussed in § 2144.09 (VI) of the MPEP:

> If the prior art does not teach any ***specific or significant utility*** for the disclosed compounds, then the prior art is unlikely to render structurally similar claims prima facie obvious in the absence of any reason for one of ordinary skill in the art to make the reference compounds or any structurally related compounds. *In re Stemniski*, 444 F.2d 581, 170 USPQ 343 (CCPA 1971).

Thus, *In re Stemniski* addresses the same situation as is presented here. Wang et al. suggest preparing antibodies from one of over 36,000 different polypeptides ('polypeptides of SEQ ID NOs: 42398-78581'; pg. 1527, WO 02/077183), which can be from one of dozens of different species of bacteria. Wang et al. do not disclose a real world use for antibodies that could be raised against the protein encoded by gene # 23372, and thus these such antibodies would not have a 'specific or significant utility' as defined in the MPEP based upon the teachings in the art prior to the instant application. Therefore, it would not have been obvious under Wang et al. to select gene # 23372 from among over 36,000 polypeptides to raise antibodies against the protein encoded by gene # 23372 or to create immunogenic compositions related the protein encoded by gene # 23372 disclosed by Wang et al., and the teachings of Wang et al. do not render obvious any of current claims 9-13.

In sharp contrast to Wang et al., the current application provides a specific and substantial utility for the compositions of claims 9 – 13. The polypeptide of SEQ ID NO: 207 was discovered through experimental evidence to unexpectedly be located in the membrane of *Neisseria meningitidis*, thereby indicating its utility for use in an immunogenic composition and as a target for vaccine development. This is an important finding and it is very different from the disclosure in Wang et al., as most proteins in bacteria are not accessible to circulating antibodies in a host organism. Following the teachings of Wang et al., one having skill in the art would not know which of the tens of thousands of polypeptides it discloses would actually be useful for immunogenic

compositions and/or vaccine development. In contrast, the current application provides clear experimental information disclosing the utility of compositions related to SEQ ID NO: 207 and claims 9-13 as immunogenic compositions.

B. Rejections based on Tettelin et al.

Tettelin et al. disclose the complete genome sequence of *Neisseria meningitidis* serogroup B strain MC58, which includes the polypeptide having accession number NMB1799. Tettelin et al. do not disclose raising antibodies against the polypeptide having accession number NMB1799 from among the couple of thousand genes disclosed therein, or placing the polypeptide in an immunogenic composition with an adjuvant. The Examiner has asserted that '(i)t would have been prima facie obvious to one having ordinary skill in the art at the time that the invention was made to combine the polypeptide NMB1799 of Tettelin et al. with an adjuvant to form an immunogenic composition for making antibodies because Campbell et al. teaches that it is customary for making monoclonal antibodies to macromolecules even without a clear objective for the application of the monoclonal antibody.'

As described above, the MPEP § 2107.01 and 2144.09 (VI) clearly indicate that prior art disclosures must have a specific or significant utility in order to render later related claims obvious. In this case, even if it was obvious to combine the teachings of Tettelin et al. and Campbell to form an immunogenic composition for making antibodies against the polypeptide NMB1799 (which it was clearly not, because Tettelin et al. discloses over 2000 open reading frames, and one having skill in the art would not have been motivated select polypeptide NMB1799 from among all of those open reading frames to raise antibodies against it in particular given that the polypeptide has been annotated as a "S-adenosylmethionine synthetase," which, as a metabolic enzyme, would not be expected to be immunoaccessible), the immunogenic composition of the theoretical combination of Tettelin et al. and Campbell cannot render the present claims obvious, because even if motivate to randomly select NMB1799 from among over 2000 open reading frames to generate antibodies said composition would lack specific or significant utility as the resulting antibodies would lack any specific or significant utility other than to use to determine the utility of NMB1799 which falls under categories (A) and/or (C) of uses that are not sufficient to provide real world utility.

The making of 'monoclonal antibodies to macromolecules even without a clear objective for the application of the monoclonal antibody' lacks utility, because there is no real world use or substantial utility for the described antibodies [MPEP § 2107.01 (I)(B)]. Without a substantial utility for the antibodies, the prior art is not sufficient to render the related claims prima facie obvious [MPEP § 2144.09 (VI)]. Thus, the immunogenic composition resulting from the theoretical combination of the teachings of Tettelin et al. and Campbell cannot render the current claims obvious.

For these reasons, the applicants respectfully request that the Examiner withdraw the rejections of claims 9-13.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal form is separated from this document and the Patent and Trademark Office determines that an extension and/or other relief (such as payment of a fee under 37 C.F.R. § 1.17 (p)) is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petition and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 223002109500.

Dated: November 25, 2009

Respectfully submitted,

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